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Primary and Metastatic Rhabdomyosarcoma in the Breast: Neoplasms of Adolescent Females, a Report From the Intergroup Rhabdomyosarcoma Study

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The occurrence of rhabdomyosarcoma (RMS) primary in or metastatic to breast has been regarded as an uncommon event, associated with an unfavorable outcome. Records of 26 patients with diagnoses of breast RMS, either primary or secondary, entered in the Intergroup Rhabdomyosarcoma Study (IRS) (1972–1992) were reviewed and compared with data regarding 47 similar patients in published reports. Of the 26 IRS cases, the histologic subtype was alveolar in 24, embryonal in 1, and not determined in 1. All were female with ages ranging from 11.5 to 20.2 years (median, 15.2 years; mode, 14–16 years). This compact age distribution of both primary (n = 7) and metastatic (n = 19) breast RMS was seen in previously reported series. Among the 19 cases of RMS with initial dissemination to breast, primary tumor sites were: extremity (n = 8), nasopharynx/paranasal sinuses (n = 7), and trunk (n = 4). IRS treatment was risk-based according to site and extent of disease. Four of 7 patients with primary RMS remain disease free 2.9 to 7 years post diagnosis. Among 19 patients with RMS initially metastatic to breast, including 7 in IRS clinical group IV at original diagnosis, three are disease free at 7.6, 15.7 and 17.0 years. Conclusions: primary or metastatic RMS in breast is almost confined to adolescent females having tumors with alveolar histology. Approximately one-half of the patients with primary breast disease and 15% of those with metastatic breast disease as an initial recurrence are long-term survivors. Med. Pediatr. Oncol. 29:181–189, 1997.

Key words: rhabdomyosarcoma; alveolar; breast; adolescence

INTRODUCTION

Rhabdomyosarcoma is strikingly heterogenous in respect to the relationship of primary site to prognosis. For example, patients with gross residual RMS in the orbit have an excellent prognosis, patients with primary tumors of the extremities with similar residual-disease status have a poor outcome, and comparable patients with primary pelvic tumors have a prognosis falling between these two. Because of these major differences related to site, the natural history and cure rates associated with RMS in unusual sites are of interest.

Studies of rare tumors require the review of clinical and pathologic information on patients seen during an extended period. Fortunately, criteria for the diagnosis of RMS and recognition of its subtypes during a central review process has remained relatively unchanged since the IRS opened in 1972. With two decades of experience, including over 3,500 newly diagnosed patients with RMS in the IRS (1972–1992), it has been possible to establish RMS in breast as an entity with unusual histologic features and strinkingly age-confined incidence. Its rarity is dependent on the population under study.

MATERIALS AND METHODS

Clinical records of patients with diagnoses of breast RMS, either primary or secondary, in IRS I-III and ''pi-

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TABLE I. Primary Rhabdomyosarcoma in Breast L (Intergroup Rhabdomyosarcoma Study Series)

Case no. (year of diagnosis)	Age at diagnosis (yrs.)	Extent of disease (maximum dia.)	Clinical Gp. histology	Therapy IRS protocols regimen no.	Best response	Site, first relapse	Outcome
1 (1973)	13.6	Bilateral breast (3 cm.) + axilla + pleural fluid	IV ALV	Biopsy RT:34Gy IRS I, regimen 5	PR	Spinal, lung	DOD, 79 wks.
2 (1976)	16.9	Primary (15 cm.) + Axilla + Pleural fluid	IV ALV	Gross excision & axillary dissection 50 Gy IRS I, regimen 6	PR	Local	DOD, 42 wks. (sepsis)
3 (1982)	15.5	Primary (21 cm) + Axilla	IV ALV	Radical mastectomy IRS II, regimen 26	CR	No	NED, 252 wks.
4 (1986)	14.9	Primary (10 cm)	I EMB	Excision & axillary dissection (−) & 2nd mastectomy IRS II, regimen 31	CR	No	NED, 362 wks.
5 (1986)	16.9	Primary (8 cm)	IIB ALV	Rad. mastectomy (nodes +) IRS III, regimen 38	CR	No	NED, 365 wks.
6 (1991)	15.2	Primary (6.5 cm)	II ALV	Mastectomy and axillary n. dissection (nodes +) IRS III, regimen 38	CR	No	NED, 150 wks.
7 (1991)	15.0	Breast (multiple, unilat.) + pleural fluid & liver	IV ALV	Biopsy IRS III, regimen 39F	CR	Local 84 wks.	DOD, 124 wks.

Abbreviations: ALV = alveolar; EMB = embryonal; PR = partial response; CR = complete response; DOD = dead of disease (tumor); NED = no evidence of disease.
For details of IRS protocols, see references 1–3.

lot'' IV [1–3] were reviewed. Patients with anterior chest wall tumors not arising from breast tissue and patients with disseminated RMS, with neither a primary tumor nor an initial relapse in breast, i.e., with breast involvement only after other (usually many) sites of dissemination, were excluded. There were no males with either primary or metastatic RMS as defined above. Tissue blocks were obtained, and histologic and other studies relative to diagnoses were repeated. All specimens were blindly reviewed by two pathologists (H.S. and T.J.T.), and the tumors were classified into histologic subtypes, i.e., embryonal and alveolar. There was a complete concordance in determining subtypes between the two pathologists and the original IRS reviewers. Among the alveolar RMS tumors, those having characteristic cytologic features but lacking a classical alveolar pattern were identified as a ''solid'' variant [4].

Twenty-six patients with primary or metastatic breast RMS were eligible for inclusion in the study group and their hospital records were reviewed in detail. All patients were treated initially by IRS I-III protocols [1–3] and by institutional and cooperative group protocols after relapse. Age at diagnosis, age at relapse (when applicable), and survival data were collected and values calculated (Tables I and II).

MEDLINE, CANCERLIT, EMBASE, BIOSIS, and the SCIENCE INDEX were used to identify reports referable to patients with RMS of breast, primary or metastatic, published since 1979, including patients of all ages. This search was confined to reports in English or those with English summaries. Inquires were made regarding reports of RMS in breast appearing in European and Japanese language publications by correspondence with authorities in these areas.

RESULTS

Basis for the histologic diagnosis in sections from these 26 tumors were reexamined. Histologic subtype included alveolar (n = 24), embryonal (n = 1), and RMS with insufficient tissue to determine the subtype (n = 1). Among the alveolar tumors, 9 were believed to exhibit the characteristics described by Tsokos et al. [4] as ''solid'' alveolar RMS.

Age at diagnosis for all patients ranged from 11.5 years to 20.2 years (mean, 15.2 years; median, 15.2 years) (Fig. 1). The age range for patients with primary breast RMS was 13.6 years to 16.9 years (mean, 15.4 years; median, 15.2 years, which was similar to the age at diagnosis among patients with diverse primary RMS and subsequent initial metastatic breast disease (range, 11.5 to 20.2 years; mean, 15.2 years; median, 15.0 years). The age of patients at time of relapse in breast among those with extramammary primary tumors ranged from 12.8 to 21.2 years (mean, 16.2 years; median, 15.8 years).

Patients entered in the IRS (1972–1992) with RMS in

TABLE II. Rhabdomyosarcoma Metastatic to Breast (Intergroup Rhabdomyosarcoma Study Series)

	IRS Clinical Group of Patients at Original Diagnosis of (Primary) RMS				
Characteristics	I (N-2)	II (N-1)	III (N-9)	IV (N-7)	Total (N-19)
Histology					
Alveolar	2	1	9	6	18
Embryonal	0	0	0	0	0
Insufficient tissue to determine subtype	0	0	0	1	1
Site of primary RMS					
Extremities	0	1	4	3	8
Nasopharynx & paranasal sinuses	2	0	3	2	7
Trunk	0	0	2	2	4
Response of primary disease[a] to therapy					
CR achieved	2	1	9	3	15
Disease-free interval	69 wks. & 133 wks.	155 wks.	43 wks.–105 wks. (Median, 79 wks.)		
Site of initial relapse (12 pts. with CR achieved in Gps. I–III)					
Breast only; + axilla( )	2 (1)		8		10
Breast + local recurrence		1			1
Bilateral breast			1		1
Subsequent sites of relapse					
Lung	1		3		4
Other breast			4		4
Trunk			2	1	3
Skeletal muscle (distant)	1		1		2
Local				1	1
Pelvis			1		1
Current status (19 pts.)					
Dead of disease (DOD)	168 wks.[b]	346 wks.	62 wks., 105 wks. 123 wks., 123 wks., 223 wks.[b] 105 wks.[c]	23 wks., 46 wks., 51 wks., 94 wks., 288 wks.	13
Alive with disease (AWD) (On R_x)			105 wks., 130 wks.	121 wks.	3
No evidence of disease (NED)	813 wks.		883 wks.	393 wks.	3

[a]Not breast mass.
[b]Patients achieving a second CR, following relapse in breast, now DOD.
[c]Known to have died sometime after relapse at 105 wks.

all sites included 1,399 females, of which 423 were in the age range 11 to 21 years at diagnosis. Among these 423 females, relapse occurred in 202. In this patient subgroup, metastasis at diagnoses or initial metastatic relapse occurred most frequently in lung sites (58 patients), followed by bone marrow (30 patients), central nervous system (22 patients), and then breast (19 patients). In 7 of the latter, metastases to breast was present at diagnosis (IRS group IV), while in 12, it occurred as a form of relapse. In 7 of these 12 it was the only recognized site of relapse. In the same subgroup of 423 female patients, 7 (1.6%) had primary breast RMS.

Among patients with primary breast RMS, the distribution of patients by IRS clinical group was: group I, (n = 1); group II, (n = 2); and group IV, (n = 4). Among patients with RMS in breast as a presentation of initial metastatic disease, the distribution according to clinical group at the time of original (not breast) diagnosis was: group I, (n = 2); group II, (n = 1); group III (n = 9) and group IV, (n = 7).

The racial-ethnic origins of these patients were: non-Hispanic Caucasian (20), African American (4), and Hispanic (2). There were no signs of symptoms of sexual precocity or history of hormone therapy noted in any of the subjects. Two had a history of prior cystic disease of the breast without biopsy. One mother had received ''hormone'' therapy during a subject's gestation because of prior spontaneous abortions.

Among the 7 patients with primary RMS of breast (Table I), there was a prevalence of alveolar histology (6 pts.), large tumors (3 with maximum diameter $\geqslant$10 cm), advanced stage (4 in group IV), and a high response rate, among those patients treated since 1982 (IRS II and III regimens [2,3]). All girls had entered menarche with at least one menstrual period at the time of diagnosis. The initial stated clinical diagnosis was fibroadenoma in 3 and fibrocystic disease in 1.

Among the 19 patients with metastatic RMS to breast (Table II), the histological features were alveolar in all 18 in which subtype could be determined. The sites of pri-

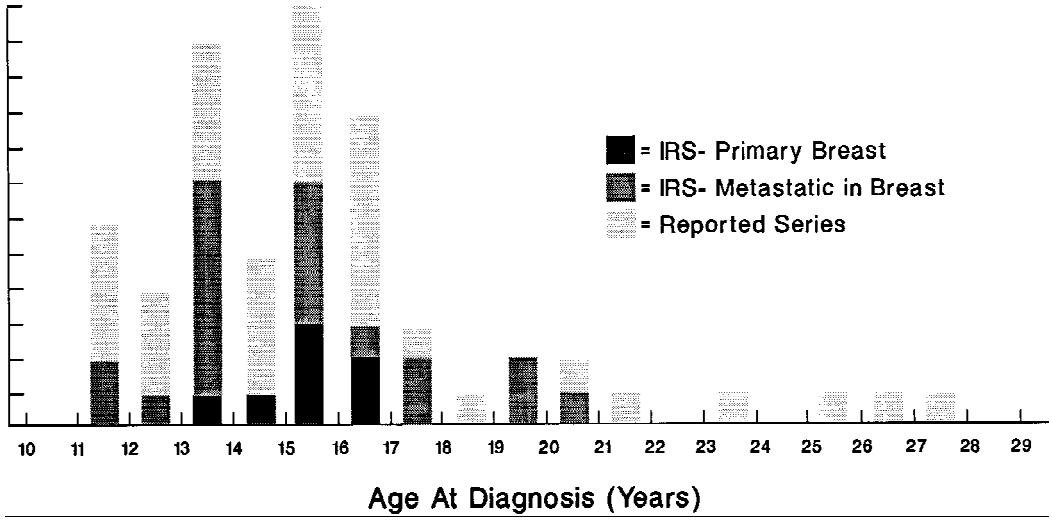

Fig. 1. Age at diagnosis of RMS among patients with primary breast RMS entered in the IRS, patients with metastatic RMS in breast (as defined) entered in the IRS, and reported patients with primary or metastatic RMS in breast published from 1980 to 1994 (see text). Four of the latter cases do not fall within the range of this graph, 2 older and 2 younger (see Table IV and text). The majority of the patients in the collected series were treated in major oncology centers (Table IV) with pathology departments that employ currently available diagnostic techniques, and with one exception, the ages at diagnosis of all patients described fall within the range of this graph.

mary RMS were confined to the extremities (n = 8), nasopharynx/paranasal (n = 7), and trunk (n = 4). One patient (age 13.6 years) had not menstruated at the time of the original diagnosis of the primary RMS but did so prior to relapse. The mean disease-free interval prior to relapse in breast was 79 ± 10 weeks (range, 43 to 155 weeks) among those 12 patients who presented with loco-regional disease (clinical groups I–III). Among these 12 patients, breast relapse occurred in 1 patient concurrent with local recurrence and in 1 as bilateral breast disease. The most frequent sites of subsequent relapse in these patients were lung and the opposite breast (Table II). After a complete response of metastatic breast lesions, 2 patients had a second relapse in extremity and trunk sites, apparently in skeletal muscle. Six patients in the total series had bilateral breast disease at some point in the course, including 3 for the first time in the setting of a *second* relapse.

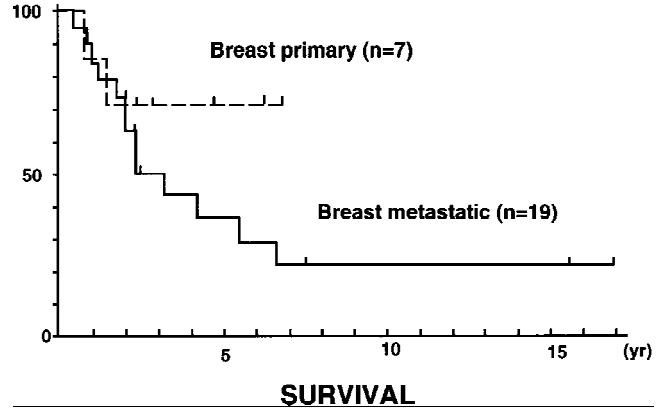

Fig. 2. Survival duration from diagnsis for patients with primary RMS of breast, and survival from time of relapse in patients with extra-mammary RMS with initial relapse in breast, employing Kaplan-Meier plot.

Response to therapy and outcome of all 26 patients are shown in Tables I and II and Figure 2. Among the 7 patients with primary RMS, 4 have no evidence of disease (NED) at 150 to 365 weeks from diagnosis. Of 12 patients with metastatic RMS in breast who were in IRS clinical groups I–III at diagnosis, 2 are NED for >15 years and 2 are alive with disease at 105 weeks and 130 weeks from diagnosis. Among the 7 patients with extra-mammary primary RMS and metastasis to breast recognized at diagnosis (clinical group IV), 3 achieved a CR (Table II). All 3 patients subsequently relapsed, but one achieved a second CR and is a survivor (>393 weeks). Thus, in the IRS series, of the 12 patients who were in clinical groups I–III at diagnosis and who relapsed in breast, 3 survived beyond 5 years from diagnosis and 2 are long-term disease-free survivors (Table II). Both of the latter achieved a complete remission (CR) after initial breast relapse, and 1 a second CR after a second relapse in the opposite breast. Both long-term survivors subsequently had uneventful pregnancies following completion of therapy. The only patient in the IRS series with embryonal RMS is in NED status (>362 weeks).

DISCUSSION

Three features which characterize patients with breast RMS were recognized in this study. The tumors were almost entirely of the alveolar subtype. The patients with both primary and secondary breast involvement were al-

TABLE III. Primary Rhabdomyosarcoma in Breast (Patients of All Ages), Published Reports (1980–1994)

Author (year)*	Age/sex	Histology	Stage	Comments
Torres & Ferrer (1985) [34]	11F	Undiff	IV	Myoglobin+
Sugar et al. (1988) [35]	14F	Alv	IV	Immunohistochemical studies +
Pettinato et al. (1989) [36]	12F	Undiff	''Local''	Immunohistochemical studies +
Altomare et al. (1990) [37]	15F pregnant		IV	
Luna-Vega et al. (1992) [16]	16F		I	Associated with fibroadenoma (8 year survival)
Roisman et al. (1992) [38]	14.5F			
Rogers et al. (1994) [17]	14F	Alv	I	

*Not included is a 45-year-old female with ''cystosarcoma phyllodes with a rhabdomyosarcomatous stroma'' described by Barnes and Pietruszka [19].

most entirely adolescent females, and there was a high frequency of bilateral disease. In addition, metastatic disease to distant trunk and extremities, unusual dissemination sites for RMS as well as most tumors, was seen in 2 IRS patients following relapse in breast.

Other clinical features of interest include: (a) the relatively large local tumors observed in patients with both primary and initial metastatic disease (Tables I and II), and (b) the response of this form of RMS to intensive chemotherapy, irradiation, and surgery, as 77% of the 26 patients achieved a complete response at some point in the course and more than ¼ were long-term survivors.

Relative to the preponderance of RMS with alveolar histologic features in this site, the proportion of alveolar tumors among patients with RMS in all sites throughout the IRS studies has been less than 25% [1–3]. Further, alveolar RMS in trunk/extremity sites in the IRS are predominantly in males [5,6]. Among those patients in the present series with primary or secondary breast involvement (as defined), when subtype could be determined, the percentage with alveolar histology was 96%, and all were female. Recent studies have demonstrated a clear distinction between the two forms of RMS on a molecular basis. Embryonal RMS does not show readily recognizable genetic abnormalities except for loss of heterozygosity (LOH) on chromosome (11p15.5) [7,8], while alveolar RMS has a characteristic chromosomal translocation, such as t(2;13) or t(1;13), which makes PAX/FKHR fusion gene and gene product [9–11].

Combining the IRS experience with reports from other institutions published during the interval 1980 to 1994, the age at diagnosis of patients with RMS primary in breast and patients with initial metastatic RMS to breast form a normal distribution curve with a peak between 14 and 16 years of age (Fig. 1). Data on age at diagnosis from each of these 3 categories of patients plotted separately has a similar pattern. Four of the 47 reported (not IRS) patients, all females, do not fall within this curve [12–14].

Relative to patient outcome, many early studies of RMS in breast were from pathology departments and included no information on therapy or survival. However, in 1991, Vergier et al. [15], from Bordeaux (France), described metastatic RMS in the breast of 16- and 18-year-old females, 1 of whom was NED 28 months after relapse. In addition to this patient and the 7 survivors in the IRS series, other recent reports include several potential long-term survivors: Luna Vega, 1992 [16], and Rogers, 1994 [17].

Relative to the early literature on primary breast RMS, Barnes and Pietruska (1978) collected 24 cases found in reports published from 1860 to 1977 [18], all of which were described as ''pleomorphic'' tumors [19]. Reports of primary breast RMS in adult patients have been infrequent since immunohistochemical and electron microscopic studies have come into general use [20–26]. Recent collected or institutional series of adults with primary breast sarcoma consist almost entirely of patients with malignant fibrous histiocytoma, fibrosarcoma, or cystosarcoma phyllodes [27–31].

Metastasis to breast from a variety of carcinomas common to adults—primarily melanoma, carcinoma of the lung, and squamous and other carcinomas of dermal origin—are well recognized [32]. Metastatic *sarcoma* in breast has also been reported in adults, but RMS very rarely in recent decades, and then only in the youngest patients in adult series [20], possibly reflecting an increase in the recognition of other tumor types. Patients with RMS reported prior to 1980, including adolescents [18,33], have not been included in Figure 1 or Tables III and IV because of diagnostic uncertainty. Although no males with breast involvement are found in the IRS, 3 males with metastatic RMS in breast have been described, including two by Howarth et al. (ages 14 and 20 years) [39] and 1 by Kennedy et al. (age 20 years) [44]. All tumors were of the alveolar subtype.

Relative to primary breast RMS among female adolescents and young women, Pappo et al. [48] collected 10 cases reported prior to 1980, some of which included an ''element'' of RMS [49], and added 2 unreported cases, ages 16 and 21 years. More recent reports of females with primary breast RMS are listed in Table III [34–38].

Reported cases of metastatic breast RMS beginning in 1980 (Table IV) included 7 adolescents described by

TABLE IV. Non-Mammary Rhabdomyosarcoma With Metastasis to Breast (All Patient Ages) Published Reports (1980–1994)

Author (year)	Patient age (yrs)	Primary site	Histology	Metastasis present at initial diagnosis	Sites of subsequent metastasis (interval from diag.)
1. Howarth, et al. (1980)[a] (St. Jude) [39]	16	Hand	Alv	BM, breast (bilateral)	
	13	Thigh	Alv	Breast (bilateral)	
	12	Foot	''Mixed''	Osseous; nodes	Breast, multiple (13 mos.)
	11.5	Hand (lt)	Alv	Axillary nodes (lt), BM	Breast (unilat.) (32 mos.)
	16	Buttocks	Alv	Osseous; BM	Breast (unilat.) (11 mos.)
2. Woodard, et al. (1980) [40]	16		Emb		(Adjacent to fibroadenoma)
3. Bohman, et al. (1982) [41] (UCLA)	15	Calf		?	Breast (bilateral)
	25	Mandible		?	Breast (bilateral)
4. Schultz, R.E. (1982) [13]	23				
	26				
	74				
	80				
5. Copeland, et al. (1985) (M.D. Anderson) [42]	13	Perineum & nodes	Alv	No	Multiple, including breast (autopsy)
	15	Perineum	Alv	No	Breast; axillary nodes
	13	Perineum & nodes	Alv	Nodes (Clinic gp, IV)	Multiple, including breast
6. Barenzelli, et al. (1986) [43]	5 cases (23–26)				
7. Kennedy, et al. (1987) [44] (NIH)	13	Extremity	Alv (solid)		Breast only, at 1 yr (unilateral)
	15	Extremity	Alv (solid)		Breast only, at 1 yr (unilateral)
8. Pettinato, G., et al. (1989) [36]	14		Alv	?	Breast (bilateral)
	17		EMB	?	Breast (bilateral)
	20		EMB	?	Breast (bilateral)
9. Ferguson et al. (1989) [14]	3	Perineum	Alv	Breast (only)	
10. Sneige, et al. (1989) [20]	28		Alv		
11. Beattie, et al. (1990) [45] Memorial, SK, N.Y.C.	13	Nasopharynx		Breast (unilat.) (only met.)	
12. Wakley, et al. (1990) [46] Med. Col. Virginia	17	Perineum		No	Breast (unilat.) (19 mos.)
13. Vergier, et al. (1991) [15] (Bordeaux, Fr)	16	Maxillary sinus	Alv	No	Breast (unilateral)
14. Chan, K.W., et al. (1991) [47] (b. Columbia)	14	Pelvis	Alv	Multiple (treated w/BMT)	Breast (unilateral)
	15	Perirectal	Alv	Multiple (treated w/BMT)	Breast (bilateral) + primary
15. Rogers, D.A., et al. (1994) [17] (St. Jude)	12	Perineum	Alv	?	Breast; pulmonary
	16	Arm	''Primitive''	Breast (only)	
16. Pappo, et al. (1994) [48]	21	Orbit	Alv	Rt. breast (only)	Breast (lt.); axilla; neck
	16	Retroperineum	Alv	Breast (only)	CNS

[a]Two males (ages 14 and 20 years) were included in this report. A male patient, age 20 yrs., was described by Kennedy, et al. [44]. All patients in the other series in this table were females. In this table missing data is prevalent in published reports describing cytologic biopsy techniques or diagnostic radiology studies [20,36,40,46].

Howarth et al. [39] which consisted of patients with multiple sites of disease, and subsequently, a report by Copeland et al. in 1985 [42] describing 3 female patients (ages 13, 13 and 15 years) with 1 clearly having an initial recurrence confined to breast and adjacent nodes. This patient survived for 27 months from diagnosis.

In addition to RMS in adolescent breast, the multi-institutional study by Pettinado et al. [36] included 2 female patients with metastatic peripheral neuroectodermal tumors in breast, ages 13 and 16 years; and a 14-year-old girl with synovial sarcoma metastatic from an extremity to breast (only) has been described [50], sug-

gesting that a predilection for breast as a metastatic site in the adolescent female may include other neoplasms common to this age group.

Recent pertinent publications [17,47] include a report of 2 female patients (ages 14 and 15 years) with alveolar RMS primary in trunk sites who were treated by bone marrow transplantation and subsequently developed RMS in breast [47]. Metastasis to breast as the *initial* manifestation of RMS with an occult primary subsequently identified has been described [45,48].

From a clinical standpoint, delay in diagnosis is suggested by the large size of the primary breast tumors and some of the initial metastases in the IRS series (Tables I and II), although this may also reflect a stimulated growth rate. Most of the patients with primary tumors were initially regarded as having fibroadenomas and observed as such. The present study suggests that discrete solid breast masses in females in the second decade of life, with a clinical diagnosis of fibroadenomas, should be biopsied if they enlarge beyond 2 cm maximum diameter. Among some patients with a prior history of RMS, the significance of the subsequent appearance of a solitary breast mass in an adolescent female was not recognized and therapy was delayed.

Females with a history of RMS in CR status who are in the second decade are more likely to develop a breast metastasis than a metastasis to other sites, excluding lung, bone marrow, and the central nervous system.

Mammography was employed at some point in the course in the IRS patients seen since 1980 but was rarely helpful. Difficulty in recognizing metastatic breast lesions by this technique was stressed by Bohman et al. (1982) [41], in a study which included 2 female patients with metastatic breast RMS (ages 15 and 25 years). These authors noted the basic differences between the appearance of carcinoma of the breast and malignant metastatic sarcoma in breast as seen in mammograms, and the striking similarity between the latter and benign breast lesions, particularly fibroadenoma. Cytology from fine needle aspiration has been successful in identifying both primary and metastatic RMS in breast [40,46].

The frequency of metastases to adolescent female breast observed in patients with RMS suggests a site predilection. The biologic basis for this is unknown, but potential contributory factors are described. Certainly, a growth-factor mediated proliferation of breast tissue, including stroma, is well documented, and rhabdomyosarcoma cells are known to have insulin-like growth factor (IGF) receptors and are responsive to IGF-II [51–54], while breast epithelium and stroma are known to express growth factors IGF-I and IGF-II [55–57]. Thus it would appear that a favorable environment for metastatic tumor growth exists in the rapidly growing adolescent breast. Interestingly, 4 patients with primary breast RMS associated with a fibroadenoma of breast have been described [16,19]. Although fibroadenoma and cystosarcoma phylloides have been noted to have progesterone receptors but not estrogen receptors [58], we are unaware of studies demonstrating other classes of growth factors such as IGF-I and IGF-II in these tumors.

The development of the breast during the second decade of life [59] has been described as ''the coordinated action of prolactin, estrogen, progesterone, adrenal steroids, insulin, growth hormone, and thyroid hormones'' [60]. Relatively unique to this age group are the nocturnal peaks of lactogenic hormone of high amplitude [61].

Tumors whose incidence is confined by the sex and the limited age-range of the patient population, including prostatic, breast, and thyroid carcinoma, have been termed ''endocrine-controlled tumors'' by dos Santos et al. (1993) [62]. The current study suggests that RMS in breast may be included in this category.

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